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## Use of intravascular imaging in managing coronary artery disease

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### Abstract

For many years, coronary angiography has been considered "the gold standard" for evaluating patients with coronary artery disease. However, angiography only provides a planar two-dimensional silhouette of the lumen and is unsuitable for the precise assessment of atherosclerosis. With the introduction of intravascular imaging, direct visualization of the arterial wall is now feasible. Intravascular imaging modalities extend diagnostic information, thereby enabling more precise evaluation of plaque burden and vessel remodeling. Of all technologies, intravascular ultrasound (IVUS) is the most mature and widely used intravascular imaging technique. Optical coherence tomography (OCT) is an evolving technology that has the highest spatial resolution of existing imaging methods, and it is becoming increasingly widespread. These methods are useful tools for planning interventional strategies and optimizing stent deployment, particularly when stenting complex lesions. We strongly support the mandatory use of IVUS for left main percutaneous coronary intervention (PCI). In addition, it can be used to evaluate vascular

responses, including neointimal growth and strut apposition, during follow-ups. Adequately powered randomized trials are needed to support IVUS or OCT use in routine clinical practice and to answer whether OCT is superior to IVUS in reducing adverse events when used to guide PCI. The current perception and adoption of innovative interventional devices, such as bioabsorbable scaffolds, will increase the need for intravascular imaging in the future.

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**Key words:** Imaging; Ultrasonics; Optical coherence tomography; Stent; Restenosis; Thrombosis

**Core tip:** Intravascular ultrasound (IVUS) and optical coherence tomography (OCT) are imaging methods that allow the direct visualization of the arterial wall and atherosclerosis. These methods are useful tools for planning interventional strategies and optimizing stent deployment and for evaluating vascular responses during follow-ups. In this review, we focus on the potential clinical utility of IVUS and OCT in patients with coronary artery disease.

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### INTRODUCTION

Intravascular ultrasound (IVUS) is the first widely applied catheter-based imaging technology that provides valuable diagnostic information to angiography (*i.e.*, vessel and lumen dimensions, plaque burden and morphology)<sup>[1]</sup>. IVUS uses a miniaturized ultrasound transducer mounted

on the tip of a catheter. In principle, IVUS is based on the emission, attenuation, and backscattering of ultrasonic waves that are converted to electrical signals and then processed as an image. The envelope (amplitude) of the radiofrequency signal is used to form the grey-scale IVUS image. In recent years, information derived from the spectral analysis of IVUS backscattered data has been added to grey-scale reconstructions to obtain a more detailed characterization of plaque morphology as a color-coded map<sup>[2]</sup>. Three main post-processing methods for tissue characterization are virtual histology IVUS (VH-IVUS, Volcano Therapeutics, Rancho Cordova, CA, United States), iMAP-IVUS (Boston Scientific Corp, Fremont, CA, United States), and integrated backscatter IVUS (IB-IVUS)<sup>[3-5]</sup>. Intravascular palpography, which measures mechanical strain of the arterial wall and has the potential to differentiate between fibrous and fatty plaque components and detect high-stress regions<sup>[6]</sup>, is a technique that is also based on IVUS. Recently, new intravascular imaging techniques with other energy sources (*e.g.*, light) have been introduced. Optical coherence tomography (OCT) is an optical technology that is based on the emission and reflection of near-infrared light. OCT has approximately 10-fold greater resolution than ultrasound-based approaches. However, the higher resolution (10 to 15- $\mu\text{m}$  axial and 20 to 25- $\mu\text{m}$  lateral) comes at the expense of poorer penetration through blood and tissue (1 to 3 mm). Recently, the earlier time-domain OCT has been replaced by frequency-domain OCT (FD-OCT) technology to reduce ischemia during blood-free optical imaging. This technique does not require proximal balloon occlusion and allows for the comprehensive scanning of long arterial segments within a few seconds<sup>[7]</sup>. Intracoronary angioscopy is an endoscopic technology that allows direct visualization of the surface color and superficial morphology<sup>[8]</sup>. Near-infrared spectroscopy (NIRS) uses a laser light source to detect lipid-rich plaques<sup>[9]</sup>. A combined NIRS-IVUS catheter has recently been introduced; it provides simultaneous acquisition of grey-scale IVUS and identification of lipid core-containing plaques.

In this review, we focus on the potential clinical utility of IVUS and OCT in patients with coronary artery disease for planning interventions and percutaneous coronary intervention (PCI) guidance.

## ASSESSMENT OF ANGIOGRAPHIC INTERMEDIATE LESIONS

Intravascular imaging methods enable more precise assessments of lesion severity in cases of angiographic intermediate coronary lesions. Fractional flow reserve (FFR) is the gold standard for invasive assessments of the functional significance of intermediate lesions<sup>[10]</sup>; however, there have been attempts to correspond IVUS or OCT measurements to the functional significance of a stenosis.

### Relationship between IVUS measurements and FFR

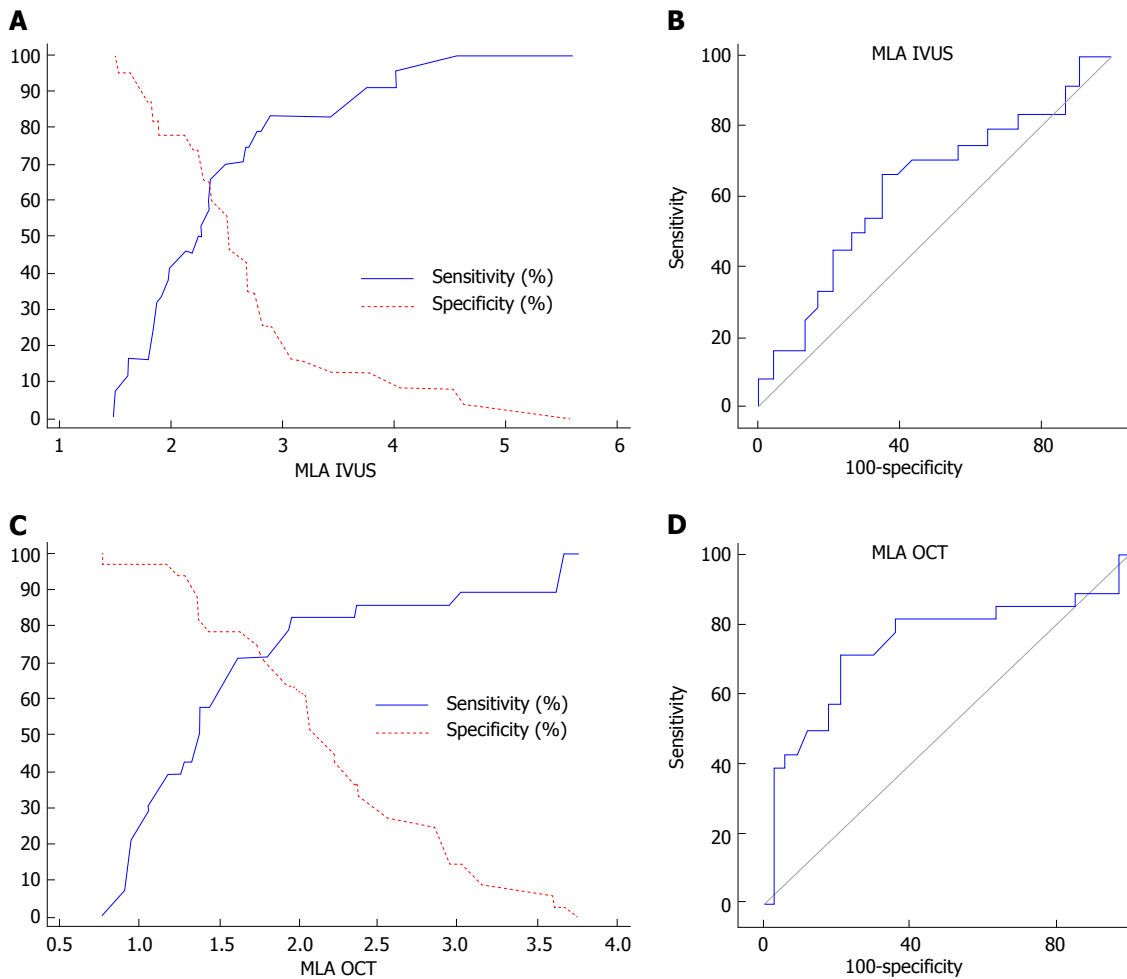
Several studies have shown good correlation between

IVUS measurements and FFR values. In a study of 53 angiographic intermediate coronary lesions, a minimum lumen area (MLA) of  $\leq 4.0 \text{ mm}^2$  (by IVUS) was reported to be the best cut-off value in identifying FFR  $< 0.75$ , with 92% sensitivity and 56% specificity<sup>[11]</sup>. Moreover, low event rates (a mean follow-up time of 13 mo) were reported in 300 patients for whom PCI was deferred on the basis of an IVUS MLA  $\geq 4.0 \text{ mm}^2$  or a minimum lumen diameter  $\geq 2.0 \text{ mm}$ , and the event rate decreased as the MLA increased<sup>[12]</sup>. An MLA cutoff of  $4.0 \text{ mm}^2$  has been the IVUS parameter that is more frequently applied in the clinical setting. However, recent studies have found different MLA cutoff values and have used a combination of other IVUS parameters to predict FFR. Recently, in a population of 201 patients with 236 coronary lesions, the best cutoff value to predict a FFR  $< 0.80$  was an MLA  $< 2.4 \text{ mm}^2$ , with a diagnostic accuracy of 68%, a high sensitivity of 90% and a poor specificity of 60%. Plaque burden and lesion length measured by IVUS were also the independent determinants for FFR<sup>[13]</sup>. An IVUS-derived MLA  $< 2.0 \text{ mm}^2$  has been reported as the best cutoff value to predict FFR  $< 0.75$  in vessels with reference diameters measuring  $< 3 \text{ mm}$ <sup>[14]</sup>.

Few studies have validated IVUS measurements as anatomic predictors for the functional significance of left main lesions. In an analysis of 55 patients, Jasti *et al.*<sup>[15]</sup> reported that an MLA of  $5.9 \text{ mm}^2$  and a minimum lumen diameter of 2.8 mm strongly predicted FFR  $< 0.75$ . In the LITRO study, which enrolled 354 patients with intermediate left main lesions, an MLA  $> 6 \text{ mm}^2$  was a safe value for deferring revascularization. In the 2-year period, there was no significant difference between the deferred and revascularized groups in terms of cardiac death-free survival (97.7% *vs* 94.5%, respectively,  $P = 0.5$ ) and event-free survival (87.3% *vs* 80.6%, respectively,  $P = 0.3$ )<sup>[16]</sup>. Recently, Kang *et al.*<sup>[17]</sup> addressed this issue in 55 patients with isolated intermediate left main lesions. The IVUS MLA value that best predicted FFR  $< 0.80$  was  $4.8 \text{ mm}^2$ , with 89% sensitivity and 83% specificity. In contrast with studies of non-left main stenosis, the specificity was acceptable high.

Based on this evidence, most intermediate non-left main lesions with an MLA  $\geq 4 \text{ mm}^2$  are non-significant, and PCI may be deferred. However, physiological evaluation is still recommended for lesions with MLA  $< 4.0 \text{ mm}^2$  because of poor specificity of IVUS parameters. Other IVUS parameters should be considered in combination with the MLA to justify revascularization, including reference vessel size, lesion length, plaque burden and area stenosis. Revascularization may be deferred in patients with left main MLA  $\geq 6.0 \text{ mm}^2$ . FFR or non-invasive stress tests should be performed for an MLA  $< 6.0 \text{ mm}^2$ . IVUS, therefore, should be used with caution as a tool to investigate the functional significance of intermediate lesions; the accuracy of IVUS measurements in predicting abnormal FFR remains debatable.

Recently the Society of Cardiovascular Angiography and Interventions released an expert consensus statement



**Figure 1** Intravascular ultrasound and optical coherence tomography derived minimum lumen area and fractional flow reserve. A: Sensitivity and specificity curve for IVUS-derived MLA to predict FFR  $\leq$  0.80; B: Receiver-operating characteristic curve for IVUS-derived MLA to predict FFR  $\leq$  0.80; C: Sensitivity and specificity curve for OCT-derived MLA to predict FFR  $\leq$  0.80; D: Receiver-operating characteristic curve for OCT-derived MLA to predict FFR  $\leq$  0.80<sup>[19]</sup>. MLA: Minimum lumen area; IVUS: Intravascular ultrasound; OCT: Optical coherence tomography; FFR: Fractional flow reserve.

on the use of FFR, IVUS, and OCT. Experts recommend using IVUS to appraise the significance of left main lesions and employing a cutoff MLA value of 6.0 mm<sup>2</sup> to assess whether revascularization is warranted. However, the use of IVUS should be discouraged when evaluating non-left main lesions<sup>[18]</sup>.

#### Relationship between OCT measurements and FFR

Few studies have examined the potential of OCT to demonstrate the functional significance of coronary artery disease and the new expert statement does not recommend using OCT to determine stenosis functional significance<sup>[18]</sup>. Recently, one study of 56 patients with 61 non-left main intermediate stenoses analyzed the value of OCT in identifying hemodynamically significant stenosis using FFR as a standard of reference. OCT showed moderate diagnostic efficiency in identifying coronary stenoses with FFR  $\leq$  0.80 (area under the curve 0.74; 95%CI: 0.61-0.84). The best OCT-derived measurements to predict FFR  $\leq$  0.80 were 1.95 mm<sup>2</sup> for the MLA (82% sensitivity, 63% specificity, and 72% accuracy) and 1.34 mm for the minimum lumen diameter (82% sensitivity, 67% specificity, and 73% accuracy). In addition 77% of

the stenoses were studied with IVUS. The IVUS cutoff value for MLA was 2.36 mm<sup>2</sup> (67% sensitivity, 65% specificity, and 66% accuracy). In patients with simultaneous IVUS and OCT, there were no significant differences in the diagnostic efficiency of OCT and IVUS, but in a subgroup of small vessels (reference diameter < 3 mm), OCT showed a significantly better diagnostic efficiency (Figure 1)<sup>[19]</sup>. The moderate diagnostic efficiency demonstrated by OCT and IVUS in this study may be related to the reference diameter of 2.60  $\pm$  0.6 mm, and 49.2% of the target vessels had reference diameters measuring < 2.5 mm. Thus, although an OCT-derived MLA may be a useful criterion for excluding hemodynamically significant stenoses, direct FFR measurements or stress tests may be necessary to identify the ischemia-inducible lesion.

## INTRAVASCULAR IMAGING FOR PCI GUIDANCE

Pre-intervention imaging provides valuable information regarding the severity of stenosis, lesion length, vessel size, and plaque characteristics. It has been used to plan

**Table 1** Intravascular ultrasound criteria for optimal stent deployment

MUSIC criteria
Complete apposition of the stent over its entire length against the vessel wall
MLA:
In-stent MLA $\geq 90\%$ of the average reference lumen area or $\geq 100\%$ of the reference segment with the lowest lumen area
In-stent MLA of proximal stent entrance $\geq 90\%$ of proximal reference lumen area
If the in-stent MLA is $> 9.0 \text{ mm}^2$ :
In-stent MLA $\geq 80\%$ of the average reference lumen area or $\geq 90\%$ of the reference segment with the lowest lumen area
In-stent MLA of proximal stent entrance $\geq 90\%$ of the proximal reference lumen area
Symmetric stent expansion defined by the minimum lumen diameter divided by the maximum lumen diameter $\geq 0.7$
AVIO study criteria
Final minimum stent cross sectional area of at least 70% of the hypothetical cross sectional area of the fully inflated balloon used for post-dilatation
The optimal balloon size that should be used for post-dilatation is the average of the media to media diameters of the distal and proximal stent segments, as well as at the sites of maximal narrowing within the stent. The value is rounded to the lowest 0.00 or 0.50 mm. For values $\geq 3.5 \text{ mm}$ , the operator could downsize the balloon diameter based on clinical judgment

MUSIC: Multicenter Ultrasound Stenting in Coronaries Study; MLA: Minimum lumen area; AVIO: Angiography *vs* IVUS Optimization; IVUS: Intravascular ultrasound.

and guide PCI and also provides information on the extent of calcium, the need for vessel preparation and the selection of device size and type. The presence of circumferential calcium can lead to plaque pretreatment with rotablation or cutting/scoring balloon prior to stent implantation. Post-intervention imaging has the potential to detect PCI complication, including the presence of edge dissections and plaque protrusion. It verifies stent expansion and apposition, as well as the need for post-dilatation or additional stent implantation. Randomized clinical studies of IVUS guidance for stent implantation have used various criteria to define an optimal result (Table 1)<sup>[20,21]</sup>.

### Impact of IVUS on restenosis and adverse events

Several post-intervention IVUS findings have been associated with restenosis and stent thrombosis. Smaller post-procedure lumen dimensions, residual reference segment stenosis, stent underexpansion, thrombus and dissections have been reported to be IVUS predictors of restenosis or stent thrombosis<sup>[22-25]</sup>.

Stent underexpansion has been the most important mechanism of stent failure (Figure 2). In a large study of 550 patients treated with sirolimus-eluting stent implantation, the target IVUS criterion for stent expansion was a post-procedural final in-stent MLA measuring  $\geq 5.0 \text{ mm}^2$  more than the distal reference segment lumen area. The only independent predictors of angiographic restenosis were final in-stent MLA by IVUS (OR = 0.586, 95%CI: 0.387-0.888,  $P = 0.012$ ) and IVUS-measured stent length (OR = 1.029, 95%CI: 1.002-1.056,  $P = 0.035$ ). The final in-stent MLA that best predicted restenosis was  $5.5 \text{ mm}^2$ <sup>[26]</sup>. In IVUS substudies of the TAXUS IV, V, and VI and TAXUS ATLAS Workhorse, Long Lesion, and Direct Stent trials, which comprised 1580 patients, the optimal thresholds of post-intervention IVUS in-stent MLA that best predicted angiographic in-stent restenosis at 9 mo were  $5.7 \text{ mm}^2$  for paclitaxel-eluting stents and  $6.4 \text{ mm}^2$  for bare metal stents (BMS)<sup>[27]</sup>. Consistent with these observations, the optimal post-intervention in-stent MLA to predict angiographic restenosis of the

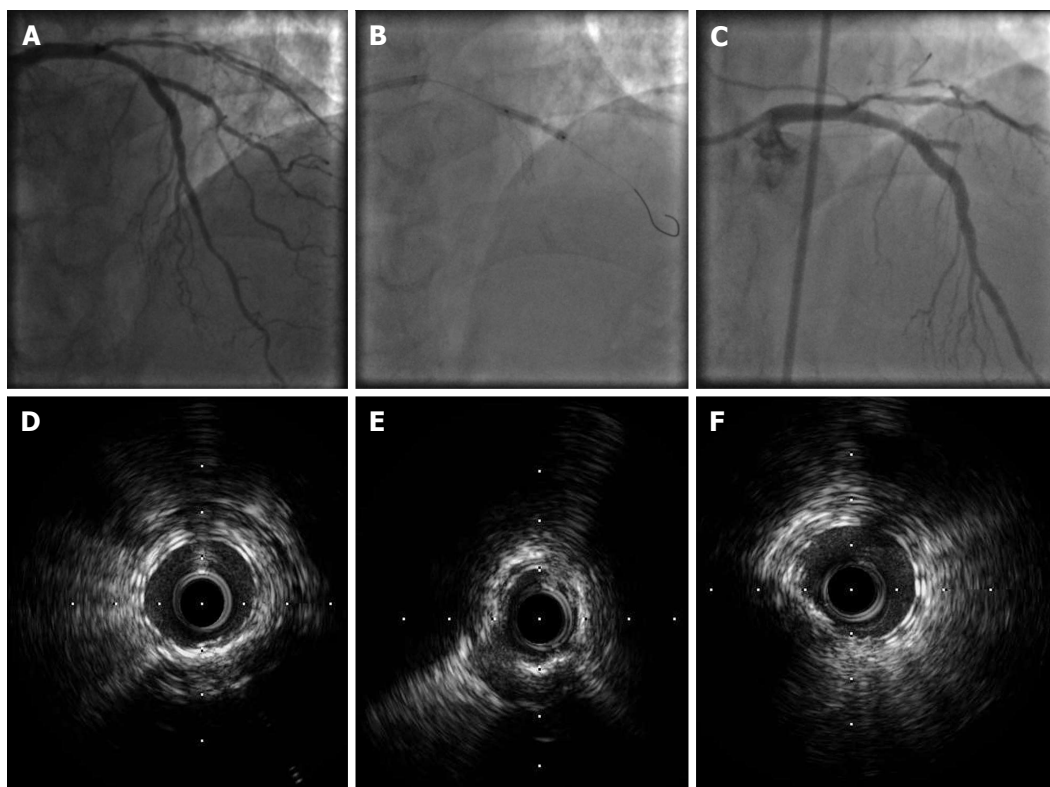
second generation drug-eluting stents was  $5.3 \text{ mm}^2$  for zotarolimus-eluting stents and  $5.4 \text{ mm}^2$  for everolimus-eluting stents<sup>[28]</sup>. However, a single cutoff value to define optimal stent implantation or to predict restenosis should be used cautiously because these studies enrolled patients with different risks for restenosis or lesion complexity.

Recently, Kang *et al.*<sup>[29]</sup> reported the best IVUS-MLA criteria that predicted angiographic in-stent restenosis on a segmental basis after left main intervention. Underexpansion was defined as post-stenting IVUS-MLA  $< 5.0 \text{ mm}^2$  at the ostial left circumflex,  $< 6.3 \text{ mm}^2$  at the ostial left anterior descending,  $< 7.2 \text{ mm}^2$  at the polygon of confluence, and  $< 8.2 \text{ mm}^2$  at the proximal left main above the polygon of confluence. Post-stenting underexpansion was an independent predictor of 2-year major adverse cardiac events, particularly repeat revascularization, while stent malapposition did not predict restenosis or major adverse cardiac events.

Few studies have reported stent malapposition as a predictor of early<sup>[30]</sup> or very late stent thrombosis<sup>[31]</sup>. However, several IVUS studies have failed to identify incomplete stent apposition as a predictor of clinical adverse events<sup>[32,33]</sup>. The IVUS substudy of the HORIZONS-AMI trial reported smaller final lumen dimensions because of tissue protrusion through stent struts and/or stent underexpansion and inflow/outflow disease (residual stenosis or stent edge dissections) but not acute malapposition as a predisposing factor of early stent thrombosis in acute myocardial infarction<sup>[34]</sup>.

### IVUS-guided PCI

In the pre-drug-eluting stent era, several studies assessed whether IVUS-guided stent implantation improves clinical outcomes compared with standard, angiography-guided PCI. However, these studies enrolled relatively small numbers of patients and were underpowered to definitively assess the role of IVUS guidance on clinical endpoints. In a meta-analysis of 7 randomized trials ( $n = 2193$ ) IVUS-guided BMS implantation was associated with a significantly lower rate of angiographic restenosis compared with angiographic-guided strategy (22% *vs*



**Figure 2** Intravascular ultrasound findings in patient with stent failure. A: Left anterior descending-Diagonal bifurcation treated with everolimus-eluting stent implantation in the left anterior descending and bioabsorbable everolimus-eluting scaffold implantation (T-stenting) in the diagonal branch; B: Post-dilatation with a noncompliant balloon in the diagonal branch; C: Four days later, the patient presented with acute myocardial infarction and stent thrombosis in the diagonal branch; D-E: Post-intervention IVUS showed stent underexpansion in the mid part of the diagonal branch (E) with good stent expansion at the proximal part (D) and at the distal part (F) of the diagonal branch. IVUS: Intravascular ultrasound.

29%, respectively,  $P = 0.02$ ), with no significant effect for myocardial infarction (3.6% *vs* 4.4%, respectively  $P = 0.51$ ) or mortality (2.4% *vs* 1.6%, respectively,  $P = 0.18$ )<sup>[35]</sup>. In a larger meta-analysis of 2972 patients, IVUS-guided strategy demonstrated a reduced risk of binary restenosis, repeat revascularization and major adverse cardiac events, without significant benefits in death or myocardial infarction<sup>[36]</sup>.

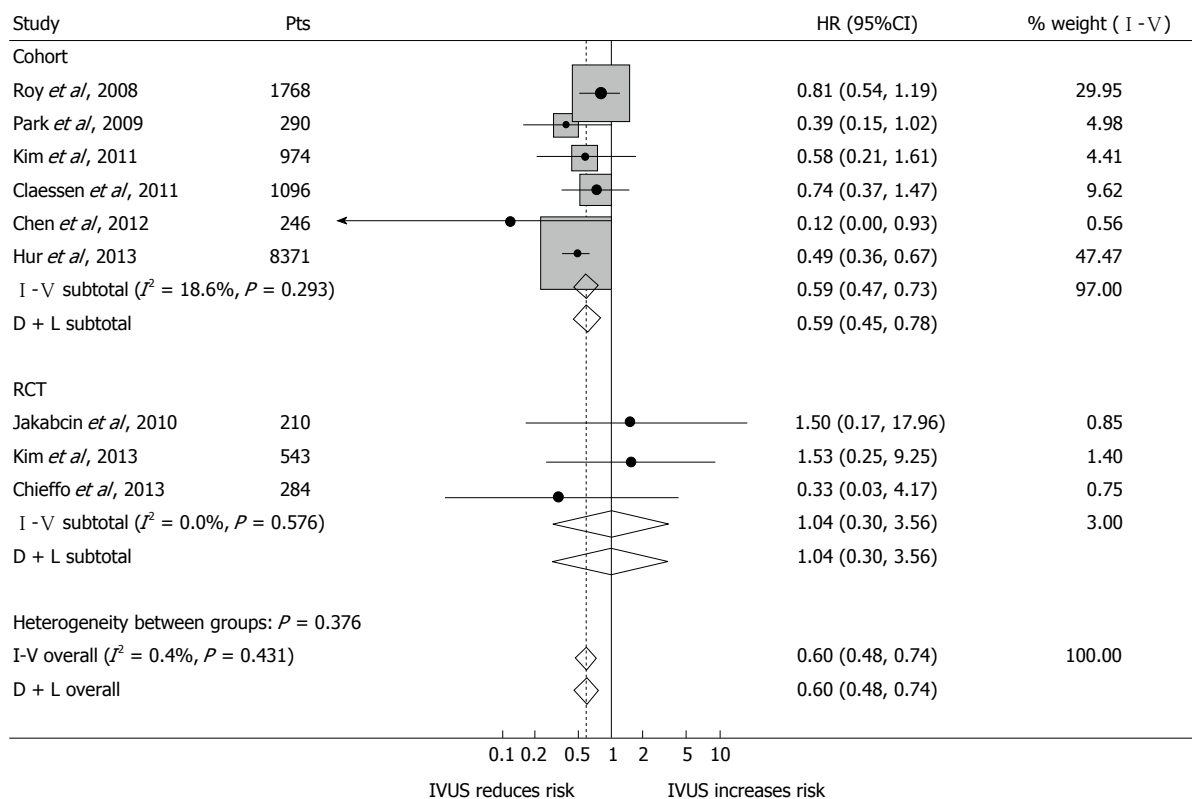
In the drug-eluting stent (DES) era, limited data from randomized trials on IVUS-guided DES are available. Recently, the Angiography *vs* IVUS Optimization (AVIO) study evaluated the safety and efficacy of IVUS *vs* angiography-guided DES post-dilatation in 284 patients with complex lesions (bifurcation, long lesions, chronic total occlusions or small vessels). IVUS guidance showed a larger final in-lesion minimum lumen diameter ( $2.70 \text{ mm} \pm 0.46 \text{ mm}$  *vs*  $2.51 \pm 0.46 \text{ mm}$ ,  $P = 0.0002$ ), with no impact on major adverse cardiac events or target lesions revascularization at 24 mo. However, an angiographic follow-up was performed in only one-third of the patients, and in this group the restenosis rates were 17.5% in the IVUS group and 28.6% in the angiography group. Moreover, the top enrollment centers had substantial experience with IVUS, and operators may develop an “IVUS eye” that leads to the ability to perform aggressive post-dilatation even with angiography guidance alone<sup>[21]</sup>. A meta-analysis of 18707 patients from 3 randomized

IVUS *vs* angiography-guided studies and 9 high quality cohort studies found that IVUS guidance reduced the risk of major adverse cardiac events (RR = 0.80, 95%CI: 0.71-0.89,  $P = 0.001$ ). This technique was associated with a reduced risk of mortality (RR = 0.60, 95%CI: 0.48-0.74,  $P = 0.001$ ), myocardial infarction (RR = 0.59, 95%CI: 0.44-0.80,  $P = 0.001$ ) and thrombosis (RR = 0.50, 95%CI: 0.32-0.80,  $P = 0.007$ ) but not of revascularization (RR = 0.95, 95%CI: 0.82-1.09,  $P = 0.75$ ) (Figure 3)<sup>[37]</sup>. This meta-analysis is supported by a recently published large-scale prospective, multicenter, non-randomized ADAPT-DES study of 8583 “all-comers” patients. In propensity adjusted multivariable analysis, IVUS guidance compared to angiography reduced the risk of stent thrombosis (0.6% *vs* 1.0%, respectively,  $P = 0.003$ ), myocardial infarction (2.5% *vs* 3.7%, respectively,  $P = 0.004$ ) and major adverse cardiac events (3.1% *vs* 4.7%, respectively,  $P = 0.002$ ) within 1 year following DES implantation<sup>[38]</sup>. IVUS guidance was particularly beneficial among patients with acute coronary syndromes and complex lesions, including left main, bifurcations and multivessel disease. In contrast, Ahmed *et al*<sup>[39]</sup> reported that the use of IVUS guidance for stent deployment failed to improve 12-mo mortality rates in patients presenting with acute myocardial infarction.

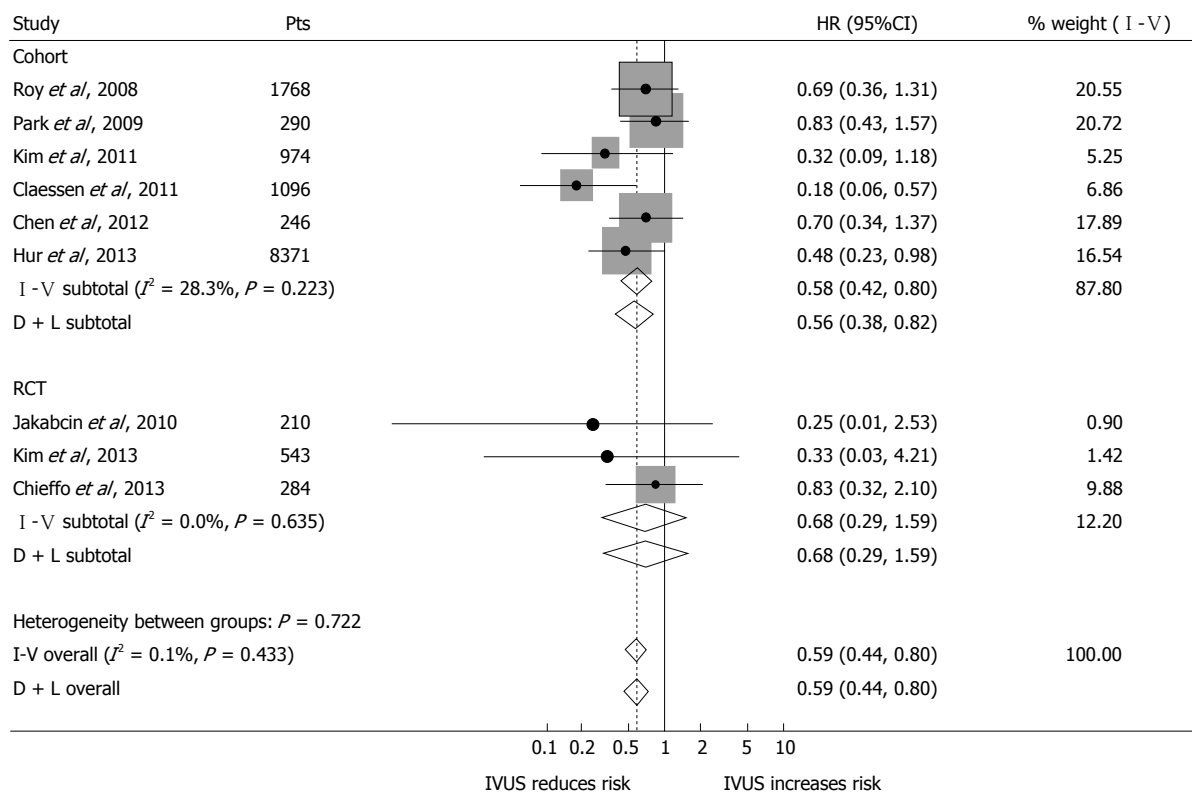
#### **IVUS-guided PCI of left main lesions**

In the MAIN-COMPARE multicenter registry, 975 pa-

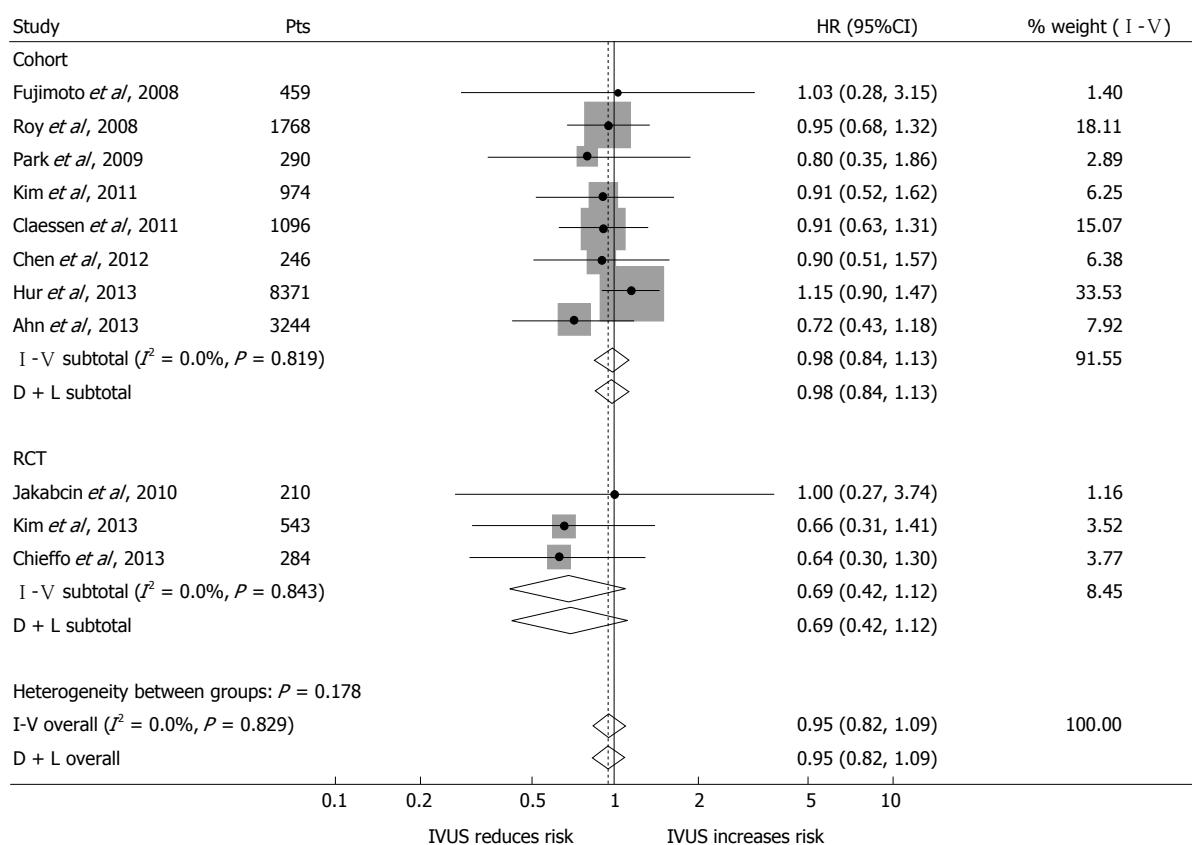
IVUS and dead (primary population)



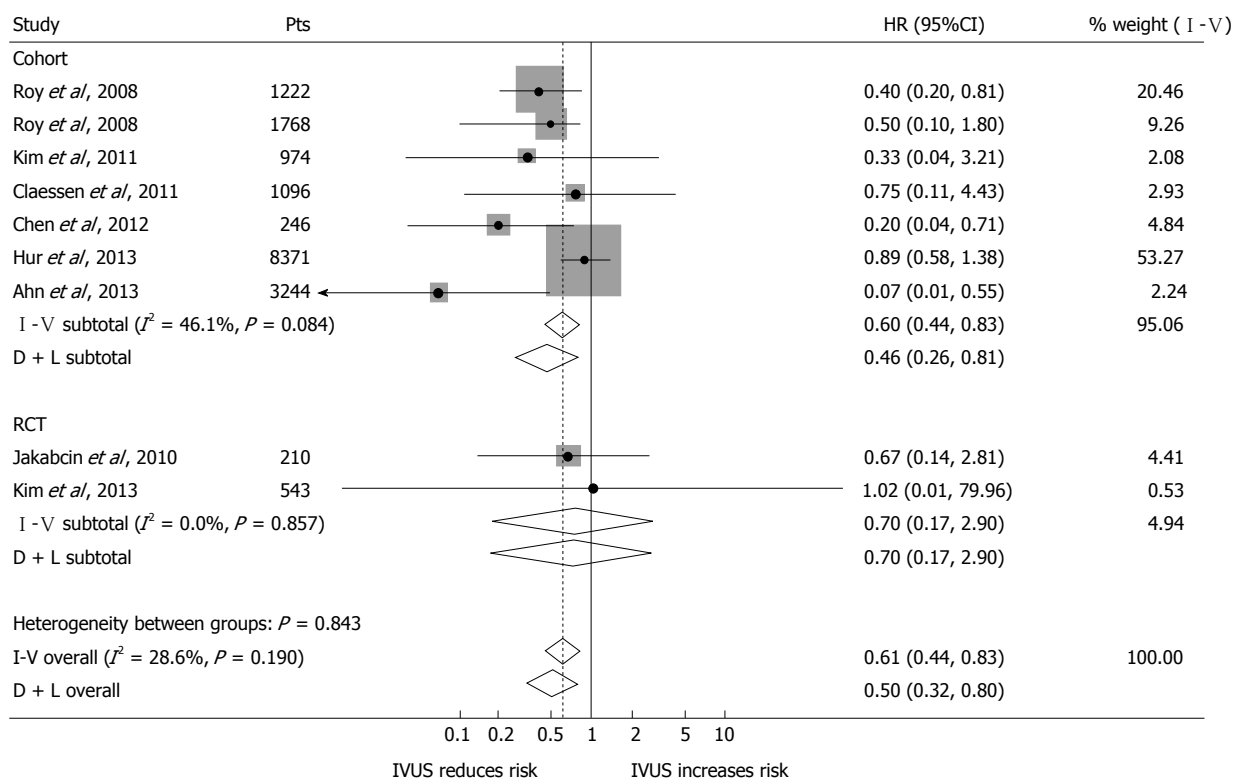
IVUS and MI (primary population)



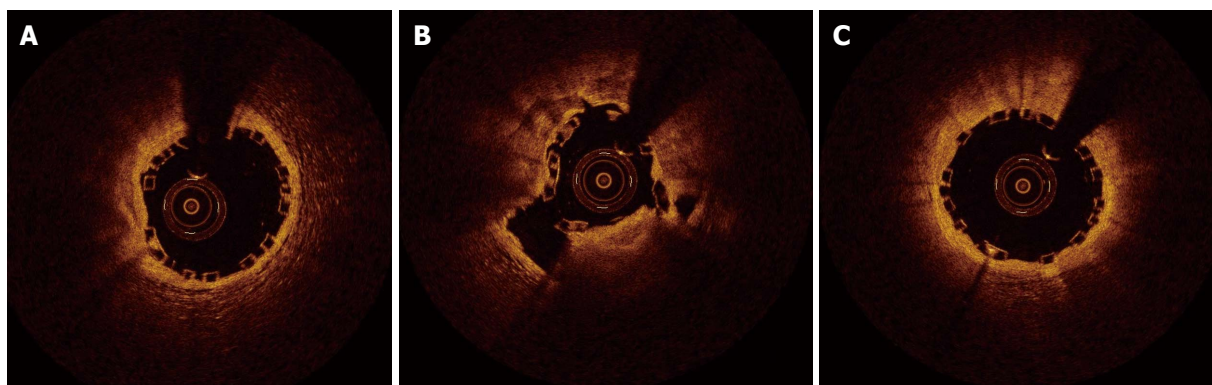
IVUS and TVR\_TLR (primary population)



IVUS and thromb (primary population)



**Figure 3 Impact of intravascular ultrasound vs angiography guidance of percutaneous coronary intervention on clinical outcomes.** A Forrest plot of the secondary endpoints [i.e., death, myocardial infarction (MI), target vessel and lesion revascularization (TVR\_TLR), thrombosis]. Diamonds represent the meta-analytic estimates and 95%CI. Adapted from [37]. IVUS: Intravascular ultrasound.



**Figure 4** Optical coherence tomography findings in patient with stent underexpansion. A-C: Post-intervention OCT of the diagonal branch after bioabsorbable scaffold implantation in a patient who presented 4 d later with stent thrombosis and acute myocardial infarction. OCT showed stent underexpansion of the mid part of the diagonal branch (B) with good stent expansion at the proximal (A) and distal (C) part of the diagonal branch. OCT: Optical coherence tomography.

tients with unprotected left main coronary artery stenosis underwent PCI under the guidance of IVUS or angiography alone. In the propensity-score matched comparison, IVUS guidance showed a trend towards lower 3-year mortality rates (6.0% in the IVUS group *vs* 13.6% in the angiography group, log-rank  $P = 0.063$ ; HR = 0.54; 95%CI: 0.28-1.03; Cox-model  $P = 0.061$ ). In particular, patients receiving DES had significantly lower mortality rates with IVUS guidance (4.7% *vs* 16.0%, log-rank  $P = 0.048$ ; HR = 0.39; 95%CI: 0.15-1.02; Cox model  $P = 0.055$ ), but after BMS implantation, the IVUS guidance did not reduce the risk of death<sup>[40]</sup>. Our Latvian randomized trial comparing paclitaxel-eluting stents to BMS in treating unprotected left main coronary artery stenosis demonstrated that PCI with IVUS guidance and cutting balloon pre-treatment is safe and effective for up to 3 years after intervention<sup>[41,42]</sup>. Therefore, we strongly support the mandatory use of IVUS for left main PCI.

Although large prospective studies appear to support IVUS-guided DES implantation, randomized trials have been underpowered to definitively assess the clinical utility of IVUS guidance because of their small sample sizes and low event rates, including restenosis or highly morbid complications.

### OCT-guided PCI

OCT has evolved from time-domain to frequency-domain imaging, which does not require proximal balloon occlusion and allows imaging of long coronary segment in a few seconds. OCT provides greater resolution than IVUS and excellent contrast between lumen and vessel wall imaging. Therefore, OCT can assess coronary plaque morphologies and identify suboptimal stent failure (*e.g.*, incomplete stent apposition, intrastent tissue protrusion, stent edge dissection, and intrastent thrombus) that is missed by IVUS. Similar to IVUS, OCT can be used to identify stent underexpansion (Figure 4). In 73 consecutive patients (80 vessels) evaluated by OCT, the incidence of edge dissection was 25%, but this incidence were not associated with clinical events during hospitalization<sup>[43]</sup>. The clinical significance of edge dissections and other parameters identified by OCT must be addressed by pro-

spective trials.

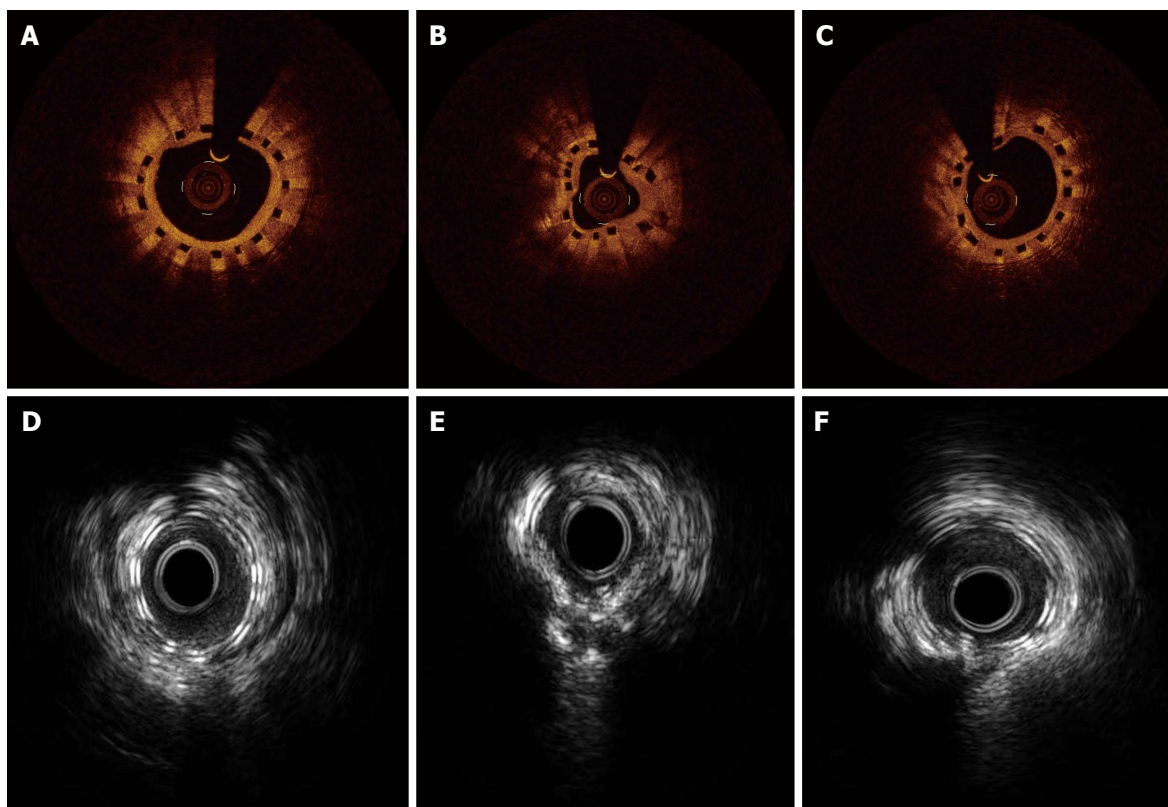
FD-OCT provides more accurate quantitative analysis of lumen. In the OPUS-CLASS study, the *in vivo* minimum lumen diameter and area measured by FD-OCT was significantly greater than those measured by quantitative coronary angiography (QCA) but smaller than those measured by IVUS. In a phantom model, the mean lumen area by FD-OCT was equal to the actual lumen area of the phantom model, while IVUS overestimated the area measurements<sup>[44]</sup>. The difference in lumen measurements between the 2 techniques is likely caused by the superior ability of FD-OCT to visualize the lumen-intima interface. Therefore, caution should be exercised before using the recommended IVUS parameters to assess lesion significance and to guide PCI by FD-OCT. The disadvantage of OCT is its limited far-field penetration. Thus, it may be more difficult to measure the true vessel size (external elastic membrane) and to identify a landing zone with the smallest plaque burden to minimize geographical miss.

In the CLI-OPCI study, Prati *et al*<sup>[45]</sup> compared OCT guidance on top of angiography for routine PCI to angiographic guidance alone in 670 patients. OCT guidance was associated with a significantly lower risk of cardiac death (3.3% *vs* 6.9%, respectively,  $P = 0.035$ ) and the composite of cardiac death, myocardial infarction, or repeat revascularization at 1 year. Thus, OCT is a safe and feasible tool for PCI guidance. However, further investigations are needed to confirm whether the use of FD-OCT will improve clinical outcomes.

### OCT vs IVUS for PCI guidance

There are ongoing discussions as to whether FD-OCT has the potential to replace IVUS for PCI guidance. In a small prospective, single center study of 70 patients, FD-OCT guidance was compared with IVUS guidance for coronary stent implantation. Although both devices showed similar accessibility and there was no significant difference for stent apposition, FD-OCT guidance demonstrated a smaller final minimum stent area, as well as smaller stent expansion and more frequent significant residual reference segment stenosis. Researchers con-





**Figure 5** Intravascular ultrasound and optical coherence tomography findings 1 yr after bioabsorbable stent implantation. A-C: The OCT findings 12 mo after bioabsorbable scaffold implantation showed complete strut coverage; D-E: IVUS also shows uncovered struts in the same patient. IVUS: Intravascular ultrasound; OCT: Optical coherence tomography.

cluded that OCT has several limitations for optimal stent deployment because of the poor visibility of the vessel border. Good vessel border visibility at the MLA site was more frequently observed in the IVUS group both prior to intervention (94.3% *vs* 8.6%,  $P < 0.001$ ) and post-intervention (94.3% *vs* 11.4%,  $P < 0.001$ ). This difference in visibility resulted in a lower frequency of post-dilatation and lower stenting and post-dilatation pressure in the OCT group<sup>[46]</sup>. Further studies are warranted to determine whether IVUS or OCT is better suited to improve clinical outcomes after stent implantation.

## EVALUATION OF NEOINTIMAL COVERAGE AFTER PCI

Intravascular imaging methods have been used to assess the vascular response to stent implantation during follow-up. Endothelial coverage is a powerful histological predictor of stent thrombosis. Post-mortem studies have shown that uncovered struts are strongly associated with late stent thrombosis<sup>[47]</sup>. With the introduction of OCT, it is possible to perform strut level analysis and to evaluate neointimal growth and stent apposition on each stent strut. Because OCT has higher resolution compared to IVUS, it is more sensitive for detailed strut-level analysis of tissue coverage and apposition (Figure 5). Stent struts are classified on OCT into four main categories: embedded-covered, protruding-covered, uncovered-

apposed, uncovered malapposed struts. In a subanalysis of the ODESSA trial, 8% of the stented segments with no detectable neointimal coverage by IVUS were found to have tissue coverage of the stent struts by OCT<sup>[48]</sup>. In a study of 34 patients (6840 struts), the prevalence of struts covered by neointima that were undetectable by IVUS was 64% at the 6-mo follow-up after sirolimus-eluting stent implantation. A total of 16% of the struts showed full coverage by neointima, whereas the average rate of neointima-covered struts in an individual stents was 89%<sup>[49]</sup>. In a formal substudy of HRORIZONS-AMI trial, OCT was performed at 13 mo in 118 patients after paclitaxel-eluting stent or BMS implantation. An analysis of 44139 struts revealed reduced neointimal hyperplasia and a greater percentage of uncovered struts, as well as higher percentage of malapposed struts in paclitaxel-eluting stents compared with BMS. While these observations are important in term of stent design, further studies are needed to determine the clinical significance of these findings<sup>[50]</sup>.

OCT also plays a critical role in assessing bioabsorbable scaffolds. OCT is capable of an accurate assessment of polymeric struts, which are seen as “boxes”, scaffold degradation and neointimal formation at follow-up<sup>[51]</sup>.

## CONCLUSION

Compared to angiography, intravascular imaging provides additional anatomic information regarding vessel wall

changes in atherosclerosis, but these methods should be used cautiously for the physiologic assessment of coronary artery disease. Therefore, the use of intravascular imaging and FFR should be complementary to guide decision making in certain coronary lesions. Because of their excellent imaging quality and spatial resolution, IVUS and OCT are the best tools for evaluating optimal stent deployment. Successful PCI of complex lesions often requires IVUS guidance, novel devices and advanced operator skills. The current perception and adoption of innovative interventional devices, such as bioabsorbable stents, will increase the need for intravascular imaging. Today, the routine use of intravascular imaging in daily practice remains controversial. Adequately powered randomized trials are needed to support IVUS or OCT use in routine clinical practice and to determine whether OCT is superior to IVUS in reducing adverse events when used to guide PCI. Selective angiography will remain vital for managing coronary artery disease. Intravascular modalities will complement rather than replace this “gold standard” and will be routinely used in selected patients. The future of intravascular imaging is the integration of functional and anatomical assessment and the usage of multiple imaging modalities in a complementary manner to diagnose and manage coronary artery disease.

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